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| 10/528,208 | 09/15/2005 | Carsten Meier | 606-42-PCT-PA | 4549 |

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| EXAMINER | |
|---|---|
| WORLEY, CATHY KINGDON | |
| ART UNIT | PAPER NUMBER |
| 1638 | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/528,208 | MEIER, CARSTEN | |
| | Examiner | Art Unit | |
| | Cathy K. Worley | 1638 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *10-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/23/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Restriction/Election*

1. In response to the communication received on April 16, 2007 from Robert Casad, Jr., the election without traverse of group I, claims 1-9, is acknowledged. The restriction requirement is MADE FINAL.

### *Specification*

2. The Applicant's amendment to the specification on Aug. 4, 2006 is acknowledged.

3. The specification is objected to because the Brief Description of the Drawings does not include a heading for the section. The Applicant is advised to amend page 8 to include - - Brief Description of the Drawings - - prior to the descriptions.

### *Information Disclosure Statement*

4. The information disclosure statement (IDS) filed Jan. 23, 2006 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because some of the

references do not include publisher, author, title, relevant pages of the publication, date, and/or place of publication. Furthermore, two of the WO documents had missing pages; therefore, the Examiner did not consider them. The paper by Isaacs et al was not provided, and therefore it was not considered. The IDS has been placed in the application file, but the information referred to in those items that were lined through by the Examiner has not been considered as to the merits. The Applicant is directed to 37 CFR 1.98 for rules on what information must be included in an IDS.

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

5. The listing of references in the specification on pages 11-12 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

*Claim Objections*

6. Claims 1 and 4 are objected to because of the following informalities:

- In claim 1, the recitation "as compared to the codes for original immunoglobulin sequences" is awkward. The Applicant is advised to amend the claim to recite - - as compared to the original nucleic acids encoding the original heavy and light chains - - , or similar language; however NEW MATTER must be avoided.
- In claim 4, there is a typographical error in line 3 of the claim. Applicant is advised to correct the spelling of "seuences". In addition, the recitation of "to enable one of cloning and purification of the protein" is awkward. The Applicant is advised to recite nucleic acids comprising restriction sites and nucleic acids encoding protein purification tags, or similar language; however NEW MATTER must be avoided. Appropriate correction is required.

7. Claims 7-9 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims are drawn to the same nucleic acid construct as the one claimed in claim 1. If the Applicant intended to claim a plant cell, plant part, or seed comprising said

nucleic acid construct, then the Applicant is advised to amend the claims accordingly.

*Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All dependent claims are included in these rejections.

Claim 1 recites the limitation "the original immunoglobulin sequences" in the last two lines of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim 1 recites the limitation "the target antigen" in line 8. There is insufficient antecedent basis for this limitation in the claim.

Claim 4 recites the limitation "the protein" in the last line of the claim. There is insufficient antecedent basis for this limitation in the claim.

9. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to nucleic acids encoding heavy and light chains of any antibody, wherein the variable region has been altered by unspecified exchanging, inserting, or deleting of any nucleotide encoding said variable regions and wherein the changes affect the encoded antibody's ability to bind to variants of any target antigen. These changes are compared to "the codes for the original immunoglobulin sequences" without any description in the specification about what "the original immunoglobulin sequences" are.

The Applicants describe oligonucleotides (see page 13, Table 1) from overlapping sequences in their particular vector (called C2200-DP-HC-LC) (see page 9 line 34). This vector, C2200-DP-HC-LC, encodes an antibody that binds to the V3 loop of the HIV-1 virus gp120 envelope protein (see page 9 lines 8-10). It is unclear from the specification that C2200-DP-HC-LC has had any alterations relative to the codes for the original immunoglobulin sequences. It appears that C2200-DP-HC-LC may encode "the original immunoglobulin sequences", although this is not expressly stated.

The Applicants have not adequately described "the codes for the original immunoglobulin sequences". Therefore, nucleic acids that have been altered relative to this original sequence have not been described. The Applicants do not describe any features of the nucleic acids that are specific to an antibody that has had the variable region altered. Nor have the Applicants described what nucleotides should be exchanged, inserted or deleted to encode antibodies that have changes in their ability to bind to variants of the target antigen. The Applicants have not described the full sequence of the vector, C2200-DP-HC-LC, nor have they provided a biological deposit which in this case would satisfy the written description requirement (see MPEP 2400). The Applicants have not described nucleic acids encoding antibodies that bind to any target protein other than the HIV gp120 protein.

The instant claims are "reach through" claims, in which the Applicant claims a prophetic product that will be obtained as the result of a process. The Applicant can not provide an adequate description of what that prophetic product is, because the Applicant does not have the product, yet.

Given the breadth of the claims, and the lack of description of specific structures associated with the instant invention, the written description requirement has not been met.

10. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acid constructs encoding heavy and light chains operably linked to promoters that function in plants does not reasonably provide enablement for nucleic acids that have been altered by exchanging, inserting or deleting one or more nucleotides compared to some undisclosed coding sequence referred to as "the codes for the original immunoglobulin sequences". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are broadly drawn to nucleic acids encoding heavy and light chains of any antibody, wherein the variable region has been altered by unspecified exchanging, inserting, or deleting of any nucleotide encoding said variable regions

and wherein the changes affect the encoded antibody's ability to bind to variants of any target antigen. These changes are compared to "the codes for the original immunoglobulin sequences" without any disclosure in the specification about what "the original immunoglobulin sequences" are.

The nature of the invention is a prophetic nucleic acid construct that encodes a prophetic antibody with altered binding to its target protein. This is a "reach through" claim, in which the Applicant teaches a process to make a particular product (in the instant case a nucleic acid construct), and the Applicant claims the product that will be made by the process.

Applicants teach oligonucleotides (see page 13, Table 1) from overlapping sequences in their particular vector (called C2200-DP-HC-LC) (see page 9 line 34). This vector, C2200-DP-HC-LC, encodes an antibody that binds to the V3 loop of the HIV-1 virus gp120 envelope protein (see page 9 lines 8-10).

The Applicants have not taught the full sequence of the vector, C2200-DP-HC-LC (see section below regarding biological deposit).

Given the lack of guidance about what the "codes for the original immunoglobulin sequences" are, one of skill in the art would not know what starting material to utilize when making the instant invention. Therefore it would require an undue amount of experimentation on the part of one of skill in the art to make the invention.

*Biological Deposit*

Claim 6 is drawn to a particular vector called C2200-DP-HC-LC. This vector must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public.

If a deposit is made under the terms of the Budapest Treaty, then a statement, affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, or someone empowered to make such a statement, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by statement, affidavit or declaration, or by someone empowered to make the same, or by a statement by an attorney of record over his or her signature and registration number showing that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

Applicants' attention is directed to MPEP § 2400 in general, and specifically to MPEP § 2411.05 as well as to 37 C.F.R. § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the

deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended to include this information, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information.

Given the lack of guidance in the instant specification, undue trial and error experimentation would be required for one of skill in the art to make and use the claimed nucleic acid constructs.

Therefore, given the breadth of the claims; the lack of guidance and working examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to make and use the claimed invention, and therefore, the invention is not enabled throughout the broad scope of the claims.

*Claim Rejections - 35 USC § 102*

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-5 and 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Bouquin et al (2002) Transgenic Research, Vol. 11, pp. 115-122.

The claims are drawn to nucleic acids encoding both the heavy chain and the light chain of an antibody.

Bouquin et al teach a nucleic acid construct referred to as C3300-DP-HC-LC which is a binary vector containing terminators and the mas1'2' dual promoter from the *A. tumefaciens* Ti plasmid for driving the expression of the heavy chain and the light chain (see left column on page 117 and Figure 1 on page 116). They included a restriction site (AGATCT) (see 5' end of the LC-ba-F linker primer on page 116 in the paragraph bridging the left and right columns). This restriction site can be used "to enable one of cloning". They teach transformation of *Arabidopsis* with this vector (see left column on page 117), therefore the nucleic acid construct is in a plant cell, plant part, and a seed.

Bouquin et al do not expressly teach alterations of the nucleic acids by exchanging, inserting, or deleting one or more nucleotides as compared to "the codes for the original immunoglobulin sequences". However, the instant specification has not taught what "the codes for the original immunoglobulin sequences" are, nor has the instant specification taught any structural differences between a construct encoding an altered antibody and a construct encoding any other monoclonal antibody. Therefore, the nucleic acid constructs taught by Bouquin et al are indistinguishable from those claimed in the instant application. See In re Best, 195 USPQ 430, 433 (CCPA 1977), which teaches that where the prior art product seems to be identical to the claimed product, except that the prior art is silent as to a particularly claimed characteristic or property, then the burden shifts to Applicant to provide evidence that the prior art would neither anticipate nor render obvious

the claimed invention. Applicant is directed to MPEP 2113 [R-1] which describes "Product-by-process"

12. No Claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner is on a variable schedule but can normally be reached on M-F 10:00 - 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). /CKW/

ANNE MARIE GRUNBERG
SUPERVISORY PATENT EXAMINER